#### 212583.ST25 SEQUENCE LISTING

<110> Nickoloff, Brian Miele, Lucio

<120> METHOD AND REAGENTS FOR EPITHELIAL BARRIER FORMATION AND TREATMENT OF MALIGNANT AND BENIGN SKIN DISORDERS BY MODULATING THE NOTCH PATHWAY

<130> 212583

<140> Unassigned

<141> 2001-08-31

<150> US 60/229,614

<151> 2000-08-31

<160> 18

<170> PatentIn version 3.1

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gcc Ala	ttt Phe 1745	gtg Val	ctt Leu	ctg Le <b>u</b>	ttc Phe	ttc Phe 1750	gt <b>g</b> Val	ggc Gly	tgc Cys	ggg Gly	gtg Val 1755	ctg Leu	ctg Leu	tcc Ser	5274
	aag Lys 1760	cgc Arg	cgg Arg	cng Xaa	cag Gln	cat His 1765	ggc Gly	cag Gln	ctc Leu	tgg Trp	ttc Phe 1770	cct Pro	gag Glu	ggc Gly	5319
ttc Phe	aaa Lys 1775	٧a١	tct Ser	gag Glu	gcc Ala	agc Ser 1780	Lys	aag Lys	aag Lys	cgg Arg	cgg Arg 1785	GIU	ncc Xaa	ctc Leu	5364

ggc gag of ly Glu Gly Glu Gly Eur Lys Pro Leu Lys Asn Ser Val Gly Eur Lys Pro Leu Lys Asn Ser Asp Ser Val Gly Eur Lys Pro Leu Lys Asn Ser Asp Ser Asp Ser Val Gly Eur Met Asp Asp Asp Asp Ash Glu Typ Gly Gly Glu Asp Cle Glu								21	.2583	3.ST2	25					5409
GIV Alla Leu Met Asp Asp Asp Len Gin Ash Giu Trp Gil Asp Ciu Asp Ciu Asp Ciu Asp Ciu Thr Lys Lys Phe Arg Phe Giu Giu Pro Val Val Leu Pro 1820  gac Ctg gac gac cag aca gac cac cac cgg cag tgg act cag cag cac cac cag ship Asp Asp Asp Gin Thr Asp Leu Asp Asp Asp Gin Thr Asp Leu Asp	ggc Gly	gag Glu 1790	gac A <b>s</b> p	tcc Ser	gtg Val	ggc Gly	ctc Leu 1795	aag Lys	Pro	Leu	aag Lys	aac Asn 1800	Ala	Ser	gac Asp	3409
gac ctg gat gac gac cag aca gac gac cag cac gac aga gac gas tag gat tag gat gas gac gac gac gac gas tag gac tag gac day cas see gac gas	ggt Gly	1805					1810					TST2	gac Asp	gag Glu	gac Asp	5454
gac ctg gat gac gac cag aca gac gac cag cac gac aga gac gas tag gat tag gat gas gac gac gac gac gas tag gac tag gac day cas see gac gas	ctg Leu	gag Glu 1820	acc Thr	aag Lys	aag Lys	ttc Phe	cgg Arg 1825	ttc Phe	gag Glu	gag Glu	ccc Pro	gtg Val 1830				5499
CCC CAGE GIV GIV VAI ASP AIR 1870  CCC CAGE GIV GIV VAI ASP AIR 1870  GRASP CYS MET ASP VAI ASP	gac Asp	ctg Leu	aac	aac	cad	aca	gac Asp	cac	caa	caa	taa	act Thr	cag Gln	cag Gln	сас His	5544
ggc ct gar ggc ctg gag acg ggc ctg Gly Fhe Thr Pro 1885 cteu Met Ile Ala Ser 1890 cys Ser Gly 1900 cteu Gly Pro Asp Gly Phe Thr Pro 1885 cteu Met Ile Ala Ser 1890 cys Ser Gly 1900 cts Gly Gly Cys Ser Gly 1900 cys Ser Gly 1900 cts Gly Gly Cys Ser Gly 1900 cys Ser Gly 1900 cts Gly Gly Cys Ser Gly 1900 cys Ser Gly 1900 cts Gly Gly Cys Ser Gly 1900 cts Gly Gly Cys Ser Gly 1900 cts Gly Gly Cys Ser Gly 1900 cts Gly Cys Ser Gly 1900 cts Gly Gly Cys Ser Gly Gly Lys Ser Ala Leu His Trp	ctg Leu	gat Asp 1850	gcc Ala	gct Ala	gac Asp	ctg Leu	cgc Arg 1855	atg Met	tct Ser	gcc Ala	atg Met	gcc Ala 1860	ccc Pro	aca Thr	ccg Pro	5589
gcc gtc leu Glu Thr Gly Asp Arg Thr Gly Glu From Arg Ser Arg Ser Arg Thr Gly Glu From Arg Ser Arg Ser Arg Thr Gly Glu	ccc Pro		ggt Gly	gag Glu	gtt Val	gac Asp	gcc Ala 1870	gac Asp	tgc Cys	atg Met	gac Asp	gtc Val 1875				5634
gcc gtc acc gac ttc atc liplo as acc gac ggc ggc ggc gcc acc ctg liplo as acc gac ggc ggc gcc acc acc acc liplo as acc gac ggc ggc ggc gcc acc acc liplo as acc gcc liplo as acc gcc liplo acc ggc ggc liplo acc ggc ggc liplo acc ggc liplo acc ggc liplo acc ggc ggc liplo acc ggc ggc liplo acc ggc ggc liplo acc ggc liplo acc ggc ggc liplo acc ggc ggc liplo acc ggc ggc liplo acc ggc ggc ggc liplo acc ggc ggc liplo acc ggc ggc liplo acc ggc liplo acc ggc ggc ggc liplo acc ggc ggc ggc liplo acc ggc ggc ggc ggc ggc ggc ggc ggc ggc	ggg Gly	cct Pro 1880	gat Asp	ggc Gly	ttc Phe	acc Thr	ccg Pro 1885	ctc Leu	atg Met	atc Ile	gcc Ala	tcc ser 1890	tgc Cys	agc Ser	ggg Gly	5679
Ala Val 1910  Cag aca aca Gln Thr Asp Arg Thr Gly Glu 1935  Tac tca tca tca 1940  Gag aca aca Arg Ser Asp Ala Ala 1945  Tyr Gln Gly Ala Ser Leu His Asn 1920  Thr Ala Leu His Cag gcc gcc gcc gcc gcc gcc gcc gcc gcc g	ggc Gly	ggc Gly 1895	ctg Leu	gag Glu	acg Thr	ggc Gly	aac Asn 1900	agc Ser	gag Glu	gaa Glu	gag Glu	gag Glu 1905	gac Asp	gcg Ala	ccg Pro	5724
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Tyr Ser 1940  gat gcc Asp Ala Ala 1945  gat gcc Asp Ala Asn Ile Gln Asp Asn 1965  gct gtg tct gcc gac gca caa ggt gtc ttc cag atc Leu Ile Arg 1970  aac cga Ash Arg Ser Ala Asp Ala Gln 1975  acc cga Ash Arg Ser Ala Asp Ala Gln 1975  cca ctg atc ctg gct gct gcc cgc atg cat glat Ala Arg 1985  cca ctg atc ctg gct gcc cgc ctg atg cat glat Arg Met His Asp Ala Arg 1985  cca ctg atc ctg gct gcc cgc ctg atg cat gat glat Arg Met His Asp 1995  cca ctg atc ctg gct gcc cgc ctg atg cat gat glat Arg Met His Asp 1995  cca ctg atc ctg gct gcc cgc ctg gat glat Ala Arg Arg 1985  cca ctg atc ctg gct gcc cgc ctg gat glat Ala Arg Cleu Ala Ala Ala Val Glu gly 2010  gac ctc atc aac tca cac gcc Asp Val Asn Ala Val Asp Asp Asp Asp Asp Asp Asp Asp Cleu Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp Asp Val Asn Val Asp Asp Val Asn Val Asp Va		aca Thr 1925	gac Asp	cgc Arg	acg Thr	ggc Gly	gag Glu 1930	acc Thr	gcc Ala	ttg Leu	cac His	ctg Leu 1935	gcc Ala			5814
Asp Ala Ash Ile Gln Asp Ash 1960 Met Gly Arg Thr 1965 Leu His Ala 1955 Ser Ala Asp Ala Gln 1975 Gly Val Phe Gln Ile Leu Ile Arg 1980 Ser Ala Asp Ala Gln 1975 Gly Val Phe Gln Ile Leu Ile Arg 1980 Leu Ile Arg 1980 Ser Ala Asp Leu Asp Ala Arg Met His Asp 1980 Gly Thr Thr 1990 Ser Ala Arg Ala Arg Met His Asp 1990 Ser Ala Arg Met His Asp 1990 Ser Ala Arg Met His Asp 1995 Gly Thr Thr 1995 Ser Ala Asp Ala Ala Arg Met His Asp 1995 Ser Ala Ala Ala Arg Met His Asp 1995 Ser Ala Ala Ala Arg Met His Asp 1995 Ser Ala Asp Val Ash Ala Val Gly 2010 Met Leu Gly 2010 Ser Asp Leu Ala Ala Ala Ala Ala Ala Val Ash Ala Val Gly Ser Asp Leu Asp 2015 Ser Ala Leu His Trp Ala Ala Ala Val Ash Ash Val Ash Va	tac Tyr	Ser	Arg	tct Ser	gat Asp	gcc Ala	Αla	aag Lys	cgc Arg	ctg Leu	ctg L <b>eu</b>	Glu	Ala	agc Ser	gca Ala	5859
Ala Val Ser Ala Asp Ala Gln 1975  aac cga gc aca gac ctg gat gcc cgc atg cat gat ggy flys fall ala Asp Ala Asp Ala Asp Asp 1985  cca ctg atc ctg gct gcc cgc ctg gag ggc gly Thr Thr 1995  cca ctg atc ctg gct gcc cgc ctg gag ggc atg ctg gag ggc atg ctg flys flys follows for the first flys follows for the first flys flys flys for Ala Leu His Trp Ala Ala Ala Val Asn Asn Val A	gat Asp	gcc Ala 1955	aac Asn	atc Ile	cag Gln	gac Asp	aac Asn 1960	atg Met	ggc Gly	cgc Arg	acc Thr	ccg Pro 1965	ctg L <b>eu</b>	cat His	gcg Ala	5904
Ash Arg 1985  Cca ctg atc ctg gct gcc cgc ctg gcg gtg gag ggc atg ctg gag Met Leu Ala Ala Arg Leu Ala Val Glu Gly 2010  gac ctc atc aac tca cac gcc Asp Leu Ile Ash Ser His Ala 2025  ggc aag tcc gcc ctg cac tgg gcc gcc gcc gtg gag ggc atg ctg gag Met Leu Glu 2010  ggc aag tcc gcc ctg cac tgg gac gtc aac gcc gta gag ggc Asp Asp Asp Leu 2015  ggc aag tcc gcc ctg cac tgg gcc gcc gcc gtg aac aat gtg gat G129  ggc aag tcc gcc ctg cac tgg gcc gcc gcc gtg aac aat gtg gat G129  G1y Lys Ser Ala Leu His Trp Ala Ala Ala Val Ash Ash Val Ash	gct Ala	٧al	tct Ser	gcc Ala	gac Asp	gca Ala	caa Gln 1975	ggt Gly	gtc Val	ttc Phe	cag Gln	atc Ile 1980	ctg Leu	atc Ile	cgg Arg	5949
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Asp Leu Ile Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu 2015 2020 2025  ggc aag tcc gcc ctg cac tgg gcc gcc gcc gtg aac aat gtg gat 6129 Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp		Leŭ	Ile	ctg Leu	gct Ala	gcć Ala	Arg	Leu	gcc Ala	gtg Val	gag Glu	ggc Gly 2010	atg Met	ctg Leu	gag Glu	6039
ggc aag tcc gcc ctg cac tgg gcc gcc gcc gtg aac aat gtg gat 6129 Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val Asp 2030 2035		Leu	Ile				ĂΊa	Asp	gtc Val	aac Asn	gcc Ala	Val	Asp			6084
		Lys	tcc ser	gcc Ala	ctg Leu	cac His	tgg Trp 2035	gcc Ala	gcc Ala	gcc Ala	gtg Val	aac Asn 2040	aat Asn )	gtg Val	gat Asp	6129

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aac i Asn i		agg Arg	gag Glu	gag Glu	aca Thr	ccc Pro 2065	ctg Leu	ttt Phe	ctg Leu	gcc Ala	gcc Ala 2070	cgg Arg	gag Glu	ggc Gly	6.	219
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	atc Ile 2090	acg Thr	gat Asp	cat His	atg Met	gac Asp 2095	cgc Arg	ctg Le <b>u</b>	ccg Pro	cgc Arg	gac Asp 2100	atc Ile	gca Ala		6	309
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ctg Leu	gtg Val 2120	cgc Arg	agc Ser	ccg Pro	cag Gln	ctg Leu 2125	cac His	gga G1y	g <b>c</b> c Ala	ccg Pro	ctg Leu 2130	ggg Gly	ggc Gly	acg Thr	6	399
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	ctg Leu 2315	cag Gln	agc Ser	ggc Gly	atg Met	gtg Val 2320	ccg Pro	aac Asn	caa Gln	tac Tyr	aac Asn 2325		ctg Leu		6984
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	ctg Leu 2360	Ser				agc Ser 2365			ggc Gly		ccc Pro 2370		acc Thr		7119
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<22	3> т	he '	xaa'	at	loca	tion	1763	sta	nds	for	Gln,	Arg,	Pro	, or Leu.	

Page 11

- <221> misc\_feature
- <222> (1787)..(1787)
- <223> The 'Xaa' at location 1787 stands for Thr, Ala, Pro, or Ser.
- <220>
- <223> Constitutively Active Notch-1
- <400> 2
- Met Pro Pro Leu Leu Ala Pro Leu Leu Cys Leu Ala Leu Leu Pro Ala 1  $\phantom{\Big|}10\phantom{\Big|}$
- Leu Ala Ala Arg Gly Pro Arg Cys Ser Gln Pro Gly Glu Thr Cys Leu  $20 \hspace{0.5cm} 25 \hspace{0.5cm} 30$
- Asn Gly Gly Lys Cys Glu Ala Ala Asn Gly Thr Glu Ala Cys Val Cys 40 45
- Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu 50 60
- Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg 65 70 75
- Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro 85 90 95
- Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg
- Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg 115 120 125
- Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys 130 140
- Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala 145 150 156
- Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg 165 170 175
- Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly 180 185 190
- Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala 195 200 205

Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr 225 230 235 240 His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu 245 250 255 Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys 260 265 270 Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn 290 295 300 Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn 305 310 315 320 Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile 325 330 335 Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp 340 345 350 Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu 355 360 365Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly 370 380 Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys 385 395 400 Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys 405 410 415 Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr 420 425 430 Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg 435 440 445 Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp 450 455 460 Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro 465 470 475 480 Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser  $485 \hspace{1.5cm} 490 \hspace{1.5cm} 495$ 

Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe  $500 \hspace{0.5in} 510$ Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp 515 520 525 Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu 530 540Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly 545 550 560 Thr His Cys Glu val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His 565 570 575 Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala 610 615 620Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile 625 630 635 640 Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu 645 650 655 Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly 660 665 670 Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His 675 680 685 Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys 690 695 700 Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys 705 710 715 720 Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile 740 745 750 Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys 755 760 765

Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser 770 780 Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys 785 790 795 800 Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn  $805 \\ 810 \\ 815$ Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro 820 825 830 Cys Ala Pro Ser Pro Cys Arg Asn Gly Glu Cys Arg Gln Ser Glu 835 840 845 Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg 865 870 875 880 His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys 885 890 895 Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn 915 920 925 Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu 930 935 940 Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn 945 950 955 960 Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe 965 970 975 Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser 980 985 990 Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys 995 1000 1005 Leu Cys Pro Pro Gly Phe Thr Gly Ser Tyr Cys Gln His Val Val 1010 1015 1020Asn Glu Cys Asp Ser Arg Pro Cys Leu Leu Gly Gly Thr Cys Gln 1025 1030 1035

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Cys	Glu 1085	Cys	Pro	Ser	Gly	Trp 1090	Thr	Gly	Leu	Tyr	Cys 1095	Asp	Val	Pro
Ser	∨al 1100	ser	Cys	Glu	val	Ala 1105	Аlа	G∏n	Arg	Gln	Gly 1110	٧a٦	Asp	val
Ala	Arg 1115	Leu	Cys	Gln	His	Gly 1120	Gly	Leu	Cys	۷a٦	Asp 1125	Ala	GТу	Asn
Thr	ніs 1130	His	Cys	Arg	Cys	Gln 1135	Ala	Gly	Tyr	Thr	Gly 1140	ser	Tyr	Cys
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Ala	Thr 1160	Cys	Thr	Asp	Tyr	Leu 1165	Gly	Gly	Tyr	Ser	Cys 1170	Lys	Cys	Val
Ala	Gly 1175	Tyr	ніѕ	Gly	Val	Asn 1180	Cys	Ser	Glu	Glu	Ile 1185	Asp	Glu	Cys
Leu	ser 1190	Нis	Pro	Cys	Gln	Asn 1195	Gly	Gly	Thr	Cys	Leu 1200	Asp	Leu	Pro
Asn	Thr 1205	Tyr	Lys	Cys	Ser	Cys 1210	Pro	Arg	Gly	Thr	Gln 1215	Gly	۷al	His
Cys	Glu 1220	Ile	Asn	۷al	Asp	Asp 1225	Cys	Asn	Pro	Pro	Val 1230	Asp	Pro	Val
Ser	Arg 1235	Ser	Pro	Lys	Cys	Phe 1240	Asn	Asn	G1y	Thr	Cys 1245	۷al	Asp	Gln
۷al	Gly 1250	Gly	Tyr	Ser	Cys	Thr 1255	Cys	Pro	Pro	Gly	Phe 1260	Val	Gly	Glu
Arg	Cys 1265	Glu	Gly	Asp	Va1	Asn 1270	Glu	Cys	Leu	ser	Asn 1275		Cys	Asp
Ala	Arg 1280	Gly	Thr	Gln	Asn	Cys 1285	۷a٦	Gln	Arg	۷a٦	Asn 1290		Phe	ніѕ
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Ile	Asn 1310	Glу	Cys	Lys	Glу	Lys 1315	Pro	Cys	Lys	Asn	Gly 1320	Gly	Thr	Cys
Ala	Val 1325	Ala	Ser	Asn	Thr	Ala 1330	Arg	Glу	Phe	Ile	Cys 1335	Lys	Cys	Pro
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Gly	Ser 1355	Leu	Arg	Cys	Leu	Asn 1360	Glу	GТу	Thr	Cys	Ile 1365	Ser	GТу	Pro
Arg	Ser 1370	Pro	Thr	Cys	Leu	Cys 1375	Leu	Glу	Pro	Phe	Thr 1380	Glу	Pro	Glu
Cys	G]n 1385	Phe	Pro	Ala	Ser	Ser 1390	Pro	Cys	Leu	Glу	Gly 1395	Asn	Pro	Cys
Tyr	Asn 1400	Gln	Gly	Thr	Cys	Glu 1405	Pro	Thr	Ser	Glu	Ser 1410	Pro	Phe	Tyr
Arg	Cys 1415	Leu	Cys	Pro	Ala	Lys 1420	Phe	Asn	Gly	Leu	Leu 1425	Cys	His	Ile
Leu	Asp 1430	Tyr	Ser	Phe	Gly	Gly 1435	Glу	Ala	Gly	Arg	Asp 1440	Ile	Pro	Pro
Pro	Leu 1445	Ile	Glu	Glu	Ala	Cys 1450	Glu	Leu	Pro	Glu	Cys 1455	G∏n	Glu	Asp
Ala	Gly 1460	Asn	Lys	۷al	Cys	ser 1465	Leu	Gln	Cys	Asn	Asn 1470	Нis	Ala	Cys
Gly	Trp 1475	Asp	Gly	Gly	Asp	Cys 1480	ser	Leu	Asn	Phe	Asn 1485	Asp	Pro	Тгр
Lys	Asn 1490	Cys	Thr	Gln	Ser	Leu 1495	Gln	Cys	Trp	Lys	Tyr 1500	Phe	Ser	Asp
Gly	His 1505	Cys	Asp	Ser	Gln	Cys 1510	Asn	Ser	Ala	Gly	Cys 1515	Leu	Phe	Asp
Gly	Phe 1520	Asp	Cys	Gln	Arg	Ala 1525	Glu	Gly	Gln	Cys	Asn 1530	Pro	Leu	туг
Asp	Gln 1535	Tyr	Cys	Lys	Asp	ніs 1540	Phe	Ser	Asp	Gly	ніs 1545	Cys	Asp	Gln

								2.	LZ 30:	0.514	2.5				
(	31y	Cys 1550	Asn	Ser	Ala	Glu	Cys 1555	Glu	Trp	Asp	Glу	Leu 1560	Asp	Cys	Ala
(	31u	ніs 1565	Val	Pro	Glu	Arg	Leu 1570	Ala	ΑΊа	GТу	Thr	Leu 1575	٧a٦	۷al	٧a٦
١	√al	Leu 1580	Met	Pro	Pro	Glu	Gln 1585	Leu	Arg	Asn	Ser	ser 1590	Phe	His	Phe
ı	Leu	Arg 1595	Glu	Leu	Ser	Arg	val 1600	Leu	His	Thr	Asn	Val 1605	٧a٦	Phe	Lys
,	Arg	Asp 1610	Ala	ніѕ	GТу	Gln	G]n 1615	Met	Ile	Phe	Pro	туг 1620	Tyr	Gly	Arg
(	Glu	Glu 1625	Glu	Leu	Arg	Lys	ніs 1630	Pro	Ile	Lys	Arg	Ala 1635	Ala	Glu	Gly
	Тгр	Ala 1640	Ala	Pro	Asp	Ala	Leu 1645	Leu	Gly	Gln	٧a٦	Lys 1650	Ala	ser	Leu
	Leu	Pro 1655	Gly	Gly	Ser	Glu	Gly 1660	Gly	Arg	Arg	Arg	Arg 1665	Glu	Leu	Asp
ı	Pro	меt 1670	Asp	val	Arg	Gly	ser 1675	Ile	٧a٦	Туг	Leu	Glu 1680	Ile	Asp	Asn
,	Arg	Gln 1685	Cys	۷al	Gln	Ala	ser 1690	Ser	Gln	Cys	Phe	Gln 1695	ser	Ala	Thr
,	Asp	Val 1700	Ala	Ala	Phe	Leu	Gly 1705	Аlа	Leu	Ala	Ser	Leu 1710	Gly	Ser	Leu
	Asn	Ile 1715	Pro	Tyr	Lys	Ile	Glu 1720	Ala	۷al	Gln	Ser	Glu 1725	Thr	۷al	Glu
	Pro	Pro 1730		Pro	Αla	Gln	Leu 1735	His	Phe	Met	Tyr	Va1 1740	Аlа	Ala	Аlа
,	Ala	Phe 1745	۷al	Leu	Leu	Phe	Phe 1750	۷a٦	GТу	Cys	Gly	Val 1755	Leu	Leu	ser
	Arg	Lys 1760	Arg	Arg	Xaa	Gln	His 1765	Gly	Gln	Leu	Trp	Phe 1770	Pro	Glu	Glу
	Phe	Lys 1775	val	ser	Glu	Аlа	Ser 1780	Lys	Lys	Lys	Arg	Arg 1785	Glu	xaa	Leu
	Glу	G1u 1790		ser	۷a٦	Glу	Leu 1795	Lys	Pro	Leu	Lys	Asn 1800	Аlа	Ser	Asp

Gly Ala Leu Met Asp Asp Asn Gln Asn Glu Trp Gly Asp Glu A 1805 1810 1815	\sp
Leu Glu Thr Lys Lys Phe Arg Phe Glu Glu Pro Val Val Leu F 1820 1830	°ro
Asp Leu Asp Asp Gln Thr Asp His Arg Gln Trp Thr Gln Gln H 1835 1840 1845	нis
Leu Asp Ala Ala Asp Leu Arg Met Ser Ala Met Ala Pro Thr F 1850 1860	Pro
Pro Gln Gly Glu Val Asp Ala Asp Cys Met Asp Val Asn Val 4	٩rg
Gly Pro Asp Gly Phe Thr Pro Leu Met Ile Ala Ser Cys Ser 0 1880 1890	gly
Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu Glu Asp Ala I 1895 1900 1905	Pro
Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser Leu His 7 1910 1915 1920	Asn
Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala Ala 7 1925 1930 1935	Arg
Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser 7 1940 1945	Ala
Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His 7 1955 1960 1965	Ala
Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile 1970 1980	Arg
Asn Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr 1985 1990 1995	Thr
Pro Leu Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu 2000 2005 2010	Glu
Asp Leu Ile Asn Ser His Ala Asp Val Asn Ala Val Asp Asp 2015 2020 2025	Leu
Gly Lys Ser Ala Leu His Trp Ala Ala Ala Val Asn Asn Val 2030 2035 2040	Asp
Ala Ala Val Val Leu Leu Lys Asn Gly Ala Asn Lys Asp Met 2045 2055	Gln

				212303.3123										
Asn	Asn 2060	Arg	Glu	Glu	Thr	Pro 2065	Leu	Phe	Leu	Ala	Ala 2070	Arg	Glu	Gly
ser	Tyr 2075	Glu	Thr	ΑΊа	Lys	Va <b>1</b> 2080	Leu	Leu	Asp	нis	Phe 2085	Аlа	Asn	Arg
Asp	Ile 2090	⊤hr	Asp	His	Met	Asp 2095	Arg	Leu	Pro	Arg	As <b>p</b> 2100	Ile	Ala	Gln
Glu	Arg 2105	Met	ніѕ	His	Asp	Ile 2110	val	Arg	Leu	Leu	Asp 2115	Glu	туr	Asn
Leu	∨al 2120	Arg	Ser	Pro	Gln	Leu 2125	His	Glу	Аlа	Pro	Leu 2130	Gly	Gly	Thr
Pro	Thr 2135	Leu	Ser	Pro	Pro	Leu 2140	Cys	ser	Pro	Asn	Gly 2145	⊤yr	Leu	Gly
Ser	Leu 2150	Lys	Pro	Glу	٧a٦	Gln 2155	Gly	Lys	Lys	٧a٦	Arg 2160	Lys	Pro	Ser
Ser	Lys 2165	Gly	Leu	Ala	Cys	Gly 2170	Ser	Lys	Glu	Ala	Lys 2175	Asp	Leu	Lys
Ala	Arg 2180	Arg	Lys	Lys	Ser	Gln 2185	Asp	Glу	Lys	Gly	Cys 2190	Leu	Leu	Asp
Ser	ser 2195	Gly	Met	Leu	Ser	Pro 2200	۷a٦	Asp	Ser	Leu	G1u 2205	ser	Pro	His
Gly	Tyr 2210	Leu	Ser	Asp	۷al	Ala 2215	Ser	Pro	Pro	Leu	Leu 2220	Pro	Ser	Pro
Phe	Gln 2225	Gln	Ser	Pro	Ser	Va1 2230	Pro	Leu	Asn	His	Leu 2235	Pro	Gly	Met
Pro	Asp 2240	Thr	нis	Leu	Gly	Ile 2245	Gly	His	Leu	Asn	va1 2250	Αla	Αla	Lys
Pro	G]u 2255	Met	Αla	Ala	Leu	Gly 2260	Gly	Gly	Glу	Arg	Leu 2265	Αla	Phe	Glu
Thr	Gly 2270	Pro	Pro	Arg	Leu	Ser 2275	His	Leu	Pro	۷al	Ala 2280	Ser	Gly	Thr
Ser	Thr 2285	∨al	Leu	Gly	Ser	Ser 2290	Ser	Gly	GТу	Ala	Leu 2295	Asn	Phe	Thr
val	G]y 2300	Gly	Ser	Thr	Ser	Leu 2305	Asn	Gly	Gln	Cys	Glu 2310	Trp	Leu	Ser

Gly Ser Val Ala Pro Gly Pro Leu Ser Thr Gln Ala Pro Ser Leu 2330 2335 2340

Gln His Gly Met Val Gly Pro Leu His Ser Ser Leu Ala Ala Ser 2345 2350 2355

Ala Leu Ser Gln Met Met Ser Tyr Gln Gly Leu Pro Ser Thr Arg 2360 2365 2370

Leu Ala Thr Gln Pro His Leu Val Gln Thr Gln Gln Val Gln Pro 2375 2380 2385

Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro Ala Asn Ile 2390 2400

Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Pro Gln Pro 2405 2415

His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg Ser 2420 2430

Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val 2435

<210> 3

<211> 1218

<212> PRT

<213> Homo sapiens

<400> 3

Met Arg Ser Pro Arg Thr Arg Gly Arg Ser Gly Arg Pro Leu Ser Leu  $1 \ \ \,$ 

Leu Leu Ala Leu Leu Cys Ala Leu Arg Ala Lys Val Cys Gly Ala Ser 20 25 30

Gly Gln Phe Glu Leu Glu Ile Leu Ser Met Gln Asn Val Asn Gly Glu 35 40 45

Leu Gln Asn Gly Asn Cys Cys Gly Gly Ala Arg Asn Pro Gly Asp Arg 50 60

Lys Cys Thr Arg Asp Glu Cys Asp Thr Tyr Phe Lys Val Cys Leu Lys 65  $\phantom{000}70\phantom{000}$  70  $\phantom{0000}75\phantom{000}$  80

Glu Tyr Gln Ser Arg Val Thr Ala Gly Gly Pro Cys Ser Phe Gly Ser 85 90 95 Gly Ser Thr Pro Val Ile Gly Gly Asn Thr Phe Asn Leu Lys Ala Ser 100 105 110 Arg Gly Asn Asp Arg Asn Arg Ile Val Leu Pro Phe Ser Phe Ala Trp 115 120 125 Pro Arg Ser Tyr Thr Leu Leu Val Glu Ala Trp Asp Ser Ser Asn Asp 130 135 140 Thr Val Gln Pro Asp Ser Ile Ile Glu Lys Ala Ser His Ser Gly Met 145 150 155 160 Ile Asn Pro Ser Arg Gln Trp Gln Thr Leu Lys Gln Asn Thr Gly Val Ala His Phe Glu Tyr Gln Ile Arg Val Thr Cys Asp Asp Tyr Tyr Tyr
180 185 190 Gly Phe Gly Cys Asn Lys Phe Cys Arg Pro Arg Asp Asp Phe Phe Gly 195 200 205 His Tyr Ala Cys Asp Gln Asn Gly Asn Lys Thr Cys Met Glu Gly Trp 210 215 220 Met Gly Pro Glu Cys Asn Arg Ala Ile Cys Arg Gln Gly Cys Ser Pro 225 230 235 240Lys His Gly Ser Cys Lys Leu Pro Gly Asp Cys Arg Cys Gln Tyr Gly Trp Gln Gly Leu Tyr Cys Asp Lys Cys Ile Pro His Pro Gly Cys Val His Gly Ile Cys Asn Glu Pro Trp Gln Cys Leu Cys Glu Thr Asn Trp 275 280 285 Gly Gly Gln Leu Cys Asp Lys Asp Leu Asn Tyr Cys Gly Thr His Gln 290 295 300 Pro Cys Leu Asn Gly Gly Thr Cys Ser Asn Thr Gly Pro Asp Lys Tyr 305 310 315 320 Gln Cys Ser Cys Pro Glu Gly Tyr Ser Gly Pro Asn Cys Glu Ile Ala 325 330 335 Glu His Ala Cys Leu Ser Asp Pro Cys His Asn Arg Gly Ser Cys Lys 340 345 350

Glu Thr Ser Leu Gly Phe Glu Cys Glu Cys Ser Pro Gly Trp Thr Gly 355 360 365 Pro Thr Cys Ser Thr Asn Ile Asp Asp Cys Ser Pro Asn Asn Cys Ser 370 380 His Gly Gly Thr Cys Gln Asp Leu Val Asn Gly Phe Lys Cys Val Cys 385 390 395 400 Pro Pro Gln Trp Thr Gly Lys Thr Cys Gln Leu Asp Ala Asn Glu Cys 405 410 415Glu Ala Lys Pro Cys Val Asn Ala Lys Ser Cys Lys Asn Leu Ile Ala 420 425 430 Ser Tyr Tyr Cys Asp Cys Leu Pro Gly Trp Met Gly Gln Asn Cys Asp 435 440 445 Ile Asn Ile Asn Asp Cys Leu Gly Gln Cys Gln Asn Asp Ala Ser Cys 450 455 460 Arg Asp Leu Val Asn Gly Tyr Arg Cys Ile Cys Pro Pro Gly Tyr Ala 465 470 475 480Gly Asp His Cys Glu Arg Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys
485
490
495 Leu Asn Gly Gly His Cys Gln Asn Glu Ile Asn Arg Phe Gln Cys Leu
500 505 510 Cys Pro Thr Gly Phe Ser Gly Asn Leu Cys Gln Leu Asp Ile Asp Tyr 515 520 525 Cys Glu Pro Asn Pro Cys Gln Asn Gly Ala Gln Cys Tyr Asn Arg Ala Ser Asp Tyr Phe Cys Lys Cys Pro Glu Asp Tyr Glu Gly Lys Asn Cys Ser His Leu Lys Asp His Cys Arg Thr Thr Pro Cys Glu Val Ile Asp Ser Cys Thr Val Ala Met Ala Ser Asn Asp Thr Pro Glu Gly Val Arg 580 585 590 Tyr Ile Ser Ser Asn Val Cys Gly Pro His Gly Lys Cys Lys Ser Gln 595 600 605 Ser Gly Gly Lys Phe Thr Cys Asp Cys Asn Lys Gly Phe Thr Gly Thr

Tyr Cys His Glu Asn Ile Asn Asp Cys Glu Ser Asn Pro Cys Arg Asn 625 630 635 640 Gly Gly Thr Cys Ile Asp Gly Val Asn Ser Tyr Lys Cys Ile Cys Ser Asp Gly Trp Glu Gly Ala Tyr Cys Glu Thr Asn Ile Asn Asp Cys Ser 660 670 Gln Asn Pro Cys His Asn Gly Gly Thr Cys Arg Asp Leu Val Asn Asp 675 680 685 Phe Tyr Cys Asp Cys Lys Asn Gly Trp Lys Gly Lys Thr Cys His Ser 690 695 700 Arg Asp Ser Gln Cys Asp Glu Ala Thr Cys Asn Asn Gly Gly Thr Cys 705 710 715 720 Tyr Asp Glu Gly Asp Ala Phe Lys Cys Met Cys Pro Gly Gly Trp Glu 725 730 735 Gly Thr Thr Cys Asn Ile Ala Arg Asn Ser Ser Cys Leu Pro Asn Pro 740 745 750 Cys His Asn Gly Gly Thr Cys Val Val Asn Gly Glu Ser Phe Thr Cys 755 760 765 Val Cys Lys Glu Gly Trp Glu Gly Pro Ile Cys Ala Gln Asn Thr Asn 770 775 780 Asp Cys Ser Pro His Pro Cys Tyr Asn Ser Gly Thr Cys Val Asp Gly Asp Asn Trp Tyr Arg Cys Glu Cys Ala Pro Gly Phe Ala Gly Pro Asp Cys Arg Ile Asn Ile Asn Glu Cys Gln Ser Ser Pro Cys Ala Phe Gly 820 825 830 Ala Thr Cys Val Asp Glu Ile Asn Gly Tyr Arg Cys Val Cys Pro Pro 835 840 845 Gly His Ser Gly Ala Lys Cys Gln Glu Val Ser Gly Arg Pro Cys Ile 850 855 860 Thr Met Gly Ser Val Ile Pro Asp Gly Ala Lys Trp Asp Asp Cys 865 870 880 Asn Thr Cys Gln Cys Leu Asn Gly Arg Ile Ala Cys Ser Lys Val Trp

Cys Gly Pro Arg Pro Cys Leu Leu His Lys Gly His Ser Glu Cys Pro  $900 \hspace{0.5cm} 905 \hspace{0.5cm} 910$ 

Ser Gly Gln Ser Cys Ile Pro Ile Leu Asp Asp Gln Cys Phe Val His 915 920 925

Pro Cys Thr Gly Val Gly Glu Cys Arg Ser Ser Ser Leu Gln Pro Val 930 935 940

Lys Thr Lys Cys Thr Ser Asp Ser Tyr Tyr Gln Asp Asn Cys Ala Asn 945 950 955 960

Ile Thr Phe Thr Phe Asn Lys Glu Met Met Ser Pro Gly Leu Thr Thr 965 970 975

Glu His Ile Cys Ser Glu Leu Arg Asn Leu Asn Ile Leu Lys Asn Val 980 985 990

Ser Ala Glu Tyr Ser Ile Tyr Ile Ala Cys Glu Pro Ser Pro Ser Ala 995 1000 1005

Asn Asn Glu Ile His Val Ala Ile Ser Ala Glu Asp Ile Arg Asp 1010 1015 1020

Asp Gly Asn Pro Ile Lys Glu Ile Thr Asp Lys Ile Ile Asp Leu 1025 1030 1035

Val Ser Lys Arg Asp Gly Asn Ser Ser Leu Ile Ala Ala Val Ala 1040 1045 1050

Glu Val Arg Val Gln Arg Arg Pro Leu Lys Asn Arg Thr Asp Phe 1055 1060 1065

Leu Val Pro Leu Leu Ser Ser Val Leu Thr Val Ala Trp Ile Cys 1070 1080

Cys Leu Val Thr Ala Phe Tyr Trp Cys Leu Arg Lys Arg Arg Lys  $1085 \hspace{0.25cm} 1090 \hspace{0.25cm} 1095$ 

Pro Gly Ser His Thr His Ser Ala Ser Glu Asp Asn Thr Thr Asn 1100 1105 1110

Asn Val Arg Glu Gln Leu Asn Gln Ile Lys Asn Pro Ile Glu Lys 1115 1120 1125

His Gly Ala Asn Thr Val Pro Ile Lys Asp Tyr Glu Asn Lys Asn 1130 1135 1140

Ser Lys Met Ser Lys Ile Arg Thr His Asn Ser Glu Val Glu Glu 1145 1150 1155

Asp Asp Met Asp Lys His Gln Gln Lys Ala Arg Phe Ala Lys Gln 1160 1165 1170

Pro Ala Tyr Thr Leu Val Asp Arg Glu Glu Lys Pro Pro Asn Gly 1175 1180 1185

Thr Pro Thr Lys His Pro Asn Trp Thr Asn Lys Gln Asp Asn Arg 1190 1195 1200

Asp Leu Glu Ser Ala Gln Ser Leu Asn Arg Met Glu Tyr Ile Val 1205 1210 1215

<210> 4

<211> 1238

<212> PRT

<213> Homo sapiens

<400> 4

Leu Ala Leu Trp Val Gln Ala Ala Arg Pro Met Gly Tyr Phe Glu Leu  $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$ 

Gln Leu Ser Ala Leu Arg Asn Val Asn Gly Glu Leu Leu Ser Gly Ala 35 40 45

Cys Cys Asp Gly Asp Gly Arg Thr Thr Arg Ala Gly Gly Cys Gly His  $50 \ \ \,$ 

Asp Glu Cys Asp Thr Tyr Val Arg Val Cys Leu Lys Glu Tyr Gln Ala 65 70 75 80

Lys Val Thr Pro Thr Gly Pro Cys Ser Tyr Gly His Gly Ala Thr Pro 85 90 95

Val Leu Gly Gly Asn Ser Phe Tyr Leu Pro Pro Ala Gly Ala Ala Gly 100 105 110

Asp Arg Ala Arg Ala Arg Ala Gly Gly Asp Gln Asp Pro Gly 115 120 125

Leu Val Val Ile Pro Phe Gln Phe Ala Trp Pro Arg Ser Phe Thr Leu 130 135 140

Ile Val Glu Ala Trp Asp Trp Asp Asn Asp Thr Thr Pro Asn Glu Glu 145 150 155 160

Leu Leu Ile Glu Arg Val Ser His Ala Gly Met Ile Asn Pro Glu Asp  $165 \hspace{0.5cm} 170 \hspace{0.5cm} 175$ Arg Trp Lys Ser Leu His Phe Ser Gly His Val Ala His Leu Glu Leu 180 185 190 Gln Ile Arg Val Arg Cys Asp Glu Asn Tyr Tyr Ser Ala Thr Cys Asn 195 200 205 Lys Phe Cys Arg Pro Arg Asn Asp Phe Phe Gly His Tyr Thr Cys Asp 210 215 220Gln Tyr Gly Asn Lys Ala Cys Met Asp Gly Trp Met Gly Lys Glu Cys 225 230 235 240 Lys Glu Ala Val Cys Lys Gln Gly Cys Asn Leu Leu His Gly Gly Cys Thr Val Pro Gly Glu Cys Arg Cys Ser Tyr Gly Trp Gln Gly Arg Phe 260 265 270 Cys Asp Glu Cys Val Pro Tyr Pro Gly Cys Val His Gly Ser Cys Val 275 280 285 Glu Pro Trp Gln Cys Asn Cys Glu Thr Asn Trp Gly Gly Leu Leu Cys 290 295 300 Asp Lys Asp Leu Asn Tyr Cys Gly Ser His His Pro Cys Thr Asn Gly Gly Thr Cys Ile Asn Ala Glu Pro Asp Gln Tyr Arg Cys Thr Cys Pro  $325 \ \ 330 \ \ \ 335$ Asp Gly Tyr Ser Gly Arg Asn Cys Glu Lys Ala Glu His Ala Cys Thr 340 345 350 Ser Asn Pro Cys Ala Asn Gly Gly Ser Cys His Glu Val Pro Ser Gly 355 360 365 Phe Glu Cys His Cys Pro Ser Gly Trp Ser Gly Pro Thr Cys Ala Leu 370 375 380 Asp Ile Asp Glu Cys Ala Ser Asn Pro Cys Ala Ala Gly Gly Thr Cys 385 390 395 400 Val Asp Gln Val Asp Gly Phe Glu Cys Ile Cys Pro Glu Gln Trp Val 405 410 415 Gly Ala Thr Cys Gln Leu Asp Ala Asn Glu Cys Glu Gly Lys Pro Cys 420 425 430

Leu Asn Ala Phe Ser Cys Lys Asn Leu Ile Gly Gly Tyr Tyr Cys Asp  $435 \ \ \, 440 \ \ \, 445$ Cys Ile Pro Gly Trp Lys Gly Ile Asn Cys His Ile Asn Val Asn Asp 450 455 460 Cys Arg Gly Gln Cys Gln His Gly Gly Thr Cys Lys Asp Leu Val Asn 465 470 475 480 Gly Tyr Gln Cys Val Cys Pro Arg Gly Phe Gly Gly Arg His Cys Glu 485 490 495 Leu Glu Arg Asp Lys Cys Ala Ser Ser Pro Cys His Ser Gly Gly Leu
500 505 510 Cys Glu Asp Leu Ala Asp Gly Phe His Cys His Cys Pro Gln Gly Phe 515 520 525 Ser Gly Pro Leu Cys Glu Val Asp Val Asp Leu Cys Glu Pro Ser Pro 530 535 540 Cys Arg Asn Gly Ala Arg Cys Tyr Asn Leu Glu Gly Asp Tyr Tyr Cys 545 550 555 560 Ala Cys Pro Asp Asp Phe Gly Gly Lys Asn Cys Ser Val Pro Arg Glu Pro Cys Pro Gly Gly Ala Cys Arg Val Ile Asp Gly Cys Gly Ser Asp 580 585 590 Ala Gly Pro Gly Met Pro Gly Thr Ala Ala Ser Gly Val Cys Gly Pro 595 600 605 His Gly Arg Cys Val Ser Gln Pro Gly Gly Asn Phe Ser Cys Ile Cys 610 620 Asp Ser Gly Phe Thr Gly Thr Tyr Cys His Glu Asn Ile Asp Asp Cys Leu Gly Gln Pro Cys Arg Asn Gly Gly Thr Cys Ile Asp Glu Val Asp 645 650 655 Ala Phe Arg Cys Phe Cys Pro Ser Gly Trp Glu Gly Glu Leu Cys Asp Thr Asn Pro Asn Asp Cys Leu Pro Asp Pro Cys His Ser Arg Gly Arg 675 685 Cys Tyr Asp Leu Val Asn Asp Phe Tyr Cys Ala Cys Asp Asp Gly Trp

Lys Gly Lys Thr Cys His Ser Arg Glu Phe Gln Cys Asp Ala Tyr Thr 705 710 715 720 Cys Ser Asn Gly Gly Thr Cys Tyr Asp Ser Gly Asp Thr Phe Arg Cys 735 Ala Cys Pro Gly Trp Lys Gly Ser Thr Cys Ala Val Ala Lys Asn 740 745 750 Ser Ser Cys Leu Pro Asn Pro Cys Val Asn Gly Gly Thr Cys Val Gly 755 760 765 Ser Gly Ala Ser Phe Ser Cys Ile Cys Arg Asp Gly Trp Glu Gly Arg Thr Cys Thr His Asn Thr Asn Asp Cys Asn Pro Leu Pro Cys Tyr Asn 785 790 795 800 Gly Gly Ile Cys Val Asp Gly Val Asn Trp Phe Arg Cys Glu Cys Ala 805 810 815 Pro Gly Phe Ala Gly Pro Asp Cys Arg Ile Asn Ile Asp Glu Cys Gln  $820 \ \ \, 825 \ \ \, 830 \ \ \,$ Ser Ser Pro Cys Ala Tyr Gly Ala Thr Cys Val Asp Glu Ile Asn Gly Tyr Arg Cys Ser Cys Pro Pro Gly Arg Ala Gly Pro Arg Cys Gln Glu 850 855 860 Val Ile Gly Phe Gly Arg Ser Cys Trp Ser Arg Gly Thr Pro Phe Pro 865 870 875 880 His Gly Ser Ser Trp Val Glu Asp Cys Asn Ser Cys Arg Cys Leu Asp 895 Gly Arg Arg Asp Cys Ser Lys Val Trp Cys Gly Trp Lys Pro Cys Leu 900 905 910 Leu Ala Gly Gln Pro Glu Ala Leu Ser Ala Gln Cys Pro Leu Gly Gln 915 920 925 Arg Cys Leu Glu Lys Ala Pro Gly Gln Cys Leu Arg Pro Pro Cys Glu 930 935 940 Ala Trp Gly Glu Cys Gly Ala Glu Glu Pro Pro Ser Thr Pro Cys Leu 945 950 955 960 Pro Arg Ser Gly His Leu Asp Asn Asn Cys Ala Arg Leu Thr Leu His 965 970 975

Page 29

Phe Asn Arg Asp His Val Pro Gln Gly Thr Thr Val Gly Ala Ile Cys Ser Gly Ile Arg Ser Leu Pro Ala Thr Arg Ala Val Ala Arg Asp Arg Leu Leu Val Leu Leu Cys Asp Arg Ala Ser Ser Gly Ala Ser Ala 1010 1015 1020 Val Glu Val Ala Val Ser Phe Ser Pro Ala Arg Asp Leu Pro Asp 1025 1030 1035 Ser Ser Leu Ile Gln Gly Ala Ala His Ala Ile Val Ala Ala Ile  $1040 \hspace{0.5cm} 1045 \hspace{0.5cm} 1050 \hspace{0.5cm}$ Thr Gln  $\mbox{Arg Gly Asn Ser}$  Ser  $\mbox{Leu Leu Leu Ala Val}$  Thr Glu  $\mbox{Val}$   $\mbox{1065}$ Lys Val Glu Thr Val Val Thr Gly Gly Ser Ser Thr Gly Leu Leu  $1070 \hspace{1.5cm} 1080$ Val Pro Val Leu Cys Gly Ala Phe Ser Val Leu Trp Leu Ala Cys Glu Arg Ser Arg Leu Pro Arg Glu Glu Ser Ala Asn Asn Gln Trp Ala Pro Leu Asn Pro Ile Arg Asn Pro Ile Glu Arg Pro Gly Gly His Lys Asp Val Leu Tyr Gln Cys Lys Asn Phe Thr Pro Pro Pro 1145 1150 1155 Arg Arg Ala Asp Glu Ala Leu Pro Gly Pro Ala Gly His Ala Ala 1160 1165 1170 Val Arg Glu Asp Glu Glu Asp Glu Asp Leu Gly Arg Gly Glu Glu 1175 1180 1185 Asp Ser Leu Glu Ala Glu Lys Phe Leu Ser His Lys Phe Thr Lys 1190 1195 1200 Asp Pro Gly Arg Ser Pro Gly Arg Pro Ala His Trp Ala Ser Gly 1205 1210 1215 Pro Lys Val Asp Asn Arg Ala Val Arg Ser Ile Asn Glu Ala Arg 1220 1230

Page 30

Tyr Val Gly Lys Glu 1235

<210> 5

<211> 257

<212> PRT

<213> Homo sapiens

<400> 5

Pro Leu Ala Glu Pro Leu Ala Pro Arg Asp Val Phe Ile Ala Val Lys  $1 \hspace{1.5cm} 10 \hspace{1.5cm} 15$ 

Thr Thr Lys Lys Phe His Arg Ala Arg Leu Asp Leu Leu Leu Glu Thr  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

Trp Ile Ser Arg His Lys Glu Met Thr Phe Ile Phe Thr Asp Gly Glu 35 40 45

Asp Glu Ala Leu Ala Arg His Thr Gly Asn Val Val Ile Thr Asn Cys 50 55 60

Ser Ala Ala His Ser Arg Gln Ala Leu Ser Cys Lys Met Ala Val Glu 65 70 75 80

Tyr Asp Arg Phe Ile Glu Ser Gly Arg Lys Trp Phe Cys His Val Asp 85 90 95

Tyr Pro His Thr Leu Asp Val Tyr Val Gly Lys Pro Ser Leu Asp Arg

Pro Ile Gln Ala Met Glu Arg Val Ser Glu Asn Lys Val Arg Pro Val 130 135 140

His Phe Trp Phe Ala Thr Gly Gly Ala Gly Phe Cys Ile Ser Arg Gly 145 150 155 160

Leu Ala Leu Lys Met Ser Pro Trp Ala Ser Gly Gly His Phe Met Asn 165 170 175

Thr Ala Glu Arg Ile Arg Leu Pro Asp Asp Cys Thr Ile Gly Tyr Ile  $180 \\ 180 \\ 185$ 

Val Glu Ala Leu Leu Gly Val Pro Leu Ile Arg Ser Gly Leu Phe His 195 200 205

Ser His Leu Glu Asn Leu Gln Gln Val Pro Thr Ser Glu Leu His Glu 210 215

Gln Val Thr Leu Ser Tyr Gly Met Phe Glu Asn Lys Arg Asn Ala Val 225  $\phantom{\bigg|}230\phantom{\bigg|}235\phantom{\bigg|}$ 

His Val Lys Gly Pro Phe Ser Val Glu Ala Asp Pro Ser Arg Trp Gly 245 250 255

Asn

<210> 6

<211> 321

<212> PRT

<213> Homo sapiens

<400> 6

Met Gln Cys Arg Leu Pro Arg Gly Leu Ala Gly Ala Leu Leu Thr Leu 1  $\phantom{\bigg|}$ 

Leu Cys Met Gly Leu Leu Cys Leu Arg Tyr His Leu Asn Leu Ser Pro 25

Gln Arg Val Gln Gly Thr Pro Glu Leu Ser Gln Pro Asn Pro Gly Pro 35 40 45

Pro Lys Leu Gln Leu His Asp Val Phe Ile Ala Val Lys Thr Thr Arg 50 60

Ala Phe His Arg Leu Arg Leu Glu Leu Leu Asp Thr Trp Val Ser 65 70 75 80

Arg Thr Arg Glu Leu Thr Phe Val Phe Thr Asp Ser Pro Asp Lys Gly 85 90

Leu Gln Glu Arg Leu Gly Ser His Leu Val Val Thr Asn Cys Ser Ala 100 105 110

Glu His Ser His Pro Ala Leu Ser Cys Lys Met Ala Ala Glu Phe Asp 115 120 125

Thr Phe Leu Ala Ser Gly Leu Arg Trp Phe Cys His Val Asp Asp Asp 130 140

Asn Tyr Val Asn Pro Arg Ala Leu Leu Gln Leu Leu Arg Ala Phe Pro 145 150 155 160

Leu Ala Arg Asp Val Tyr Val Gly Arg Pro Ser Leu Asn Arg Pro Ile  $165 \hspace{1.5cm} 170 \hspace{1.5cm} 175$ 

Trp Phe Ala Thr Gly Gly Ala Gly Phe Cys Ile Asn Arg Lys Leu Ala 195 200 205

Leu Lys Met Ala Pro Trp Ala Ser Gly Ser Arg Phe Met Asp Thr Ser 210 215 220

Ala Leu Ile Arg Leu Pro Asp Asp Cys Thr Met Gly Tyr Ile Ile Glu 225 230 235 240

Cys Lys Leu Gly Gly Arg Leu Gln Pro Ser Pro Leu Phe His Ser His 245 250 255

Leu Glu Thr Leu Gln Leu Leu Arg Thr Ala Gln Leu Pro Glu Gln Val 260 265 270

Thr Leu Ser Tyr Gly Val Phe Glu Gly Lys Leu Asn Val Ile Lys Leu 275 280 285

Gln Gly Pro Phe Ser Pro Glu Glu Asp Pro Ser Arg Phe Arg Ser Leu 290 295 300

His Cys Leu Leu Tyr Pro Asp Thr Pro Trp Cys Pro Gln Leu Gly Ala 305 310 315 320

Ara

<210> 7

<211> 191

<212> PRT

<213> Homo sapiens

<400> 7

Met Ser Arg Ala Arg Gly Ala Leu Cys Arg Ala Cys Leu Ala Leu Ala 1 10 15

Ala Ala Leu Ala Ala Leu Leu Leu Pro Leu Pro Leu Pro Arg Ala 20 25 30

Pro Ala Pro Ala Arg Thr Pro Ala Pro Ala Pro Arg Ala Pro Pro Ser  $\frac{35}{40}$ 

Arg Pro Ala Ala Pro Ser Leu Arg Pro Asp Asp Val Phe Ile Ala Val 50 60

Lys Thr Thr Arg Lys Asn His Gly Pro Arg Leu Arg Leu Leu Leu Arg 65 70 75 80

Thr Trp Ile Ser Arg Ala Arg Gln Gln Thr Phe Ile Phe Thr Asp Gly 90 95

Asp Asp Pro Glu Leu Glu Leu Gln Gly Gly Asp Arg Val Ile Asn Thr  $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110 \hspace{1.5cm}$ 

Asn Cys Ser Ala Val Arg Thr Arg Gln Ala Leu Cys Cys Lys Met Ser 115 120 125

Val Glu Tyr Asp Lys Phe Ile Glu Ser Gly Arg Lys Trp Phe Cys His 130 135 140

Val Asp Asp Asp Asp Tyr Val Asn Ala Arg Ser Leu Leu His Leu Leu 145  $150\,$  155  $160\,$ 

ASP His Pro Ile Glu Ala Thr Glu Arg Val Gln Gly Gly Arg Thr 180 185 190

<210> 8

<211> 1404

<212> PRT

<213> Drosophila melanogaster

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Met Phe Arg Lys His Phe Arg Arg Lys Pro Ala Thr Ser Ser Ser Leu 1 10 15

Glu Ser Thr Ile Glu Ser Ala Asp Ser Leu Gly Met Ser Lys Lys Thr

Ala Thr Lys Arg Gln Arg Pro Arg His Arg Val Pro Lys Ile Ala Thr 35 40 45

Leu Pro Ser Thr Ile Arg Asp Cys Arg Ser Leu Lys Ser Ala Cys Asn 50 60

Leu Ile Ala Leu Ile Leu Ile Leu Leu Val His Lys Ile Ser Ala Ala 65 70 75 80

Gly Asn Phe Glu Leu Glu Ile Leu Glu Ile Ser Asn Thr Asn Ser His Leu Leu Asn Gly Tyr Cys Cys Gly Met Pro Ala Glu Leu Arg Ala Thr  $100 \hspace{0.5cm} 105 \hspace{0.5cm} 110$ Lys Thr Ile Gly Cys Ser Pro Cys Thr Thr Ala Phe Arg Leu Cys Leu 115 120 125 Lys Glu Tyr Gln Thr Thr Glu Gln Gly Ala Ser Ile Ser Thr Gly Cys 130 135 140 Ser Phe Gly Asn Ala Thr Thr Lys Ile Leu Gly Gly Ser Ser Phe Val 145 150 155 160 Leu Ser Asp Pro Gly Val Gly Ala Ile Val Leu Pro Phe Thr Phe Arg Trp Thr Lys Ser Phe Thr Leu Ile Leu Gln Ala Leu Asp Met Tyr Asn  $180 \hspace{1cm} 185 \hspace{1cm} 190$ Thr Ser Tyr Pro Asp Ala Glu Arg Leu Ile Glu Glu Thr Ser Tyr Ser 195 200 205 Gly Val Ile Leu Pro Ser Pro Glu Trp Lys Thr Leu Asp His Ile Gly 210 215 220 Arg Asn Ala Arg Ile Thr Tyr Arg Val Arg Val Gln Cys Ala Val Thr 225 230 235 240 Tyr Tyr Asn Thr Thr Cys Thr Thr Phe Cys Arg Pro Arg Asp Asp Gln 245 250 255 Phe Gly His Tyr Ala Cys Gly Ser Glu Gly Gln Lys Leu Cys Leu Asn  $260 \hspace{1.5cm} 265 \hspace{1.5cm} 270 \hspace{1.5cm}$ Gly Trp Gln Gly Val Asn Cys Glu Glu Ala Ile Cys Lys Ala Gly Cys 275 280 285 Asp Pro Val His Gly Lys Cys Asp Arg Pro Gly Glu Cys Glu Cys Arg Pro Gly Trp Arg Gly Pro Leu Cys Asn Glu Cys Met Val Tyr Pro Gly 305 310 315 320 Cys Lys His Gly Ser Cys Asn Gly Ser Ala Trp Lys Cys Val Cys Asp 325 330 335 Thr Asn Trp Gly Gly Ile Leu Cys Asp Gln Asp Leu Asn Phe Cys Gly 340 345 350

Thr His Glu Pro Cys Lys His Gly Gly Thr Cys Glu Asn Thr Ala Pro Asp Lys Tyr Arg Cys Thr Cys Ala Glu Gly Leu Ser Gly Glu Gln Cys Glu Ile Val Glu His Pro Cys Ala Thr Arg Pro Cys Arg Asn Gly Gly 385 390 395 400 Thr Cys Thr Leu Lys Thr Ser Asn Arg Thr Gln Ala Gln Val Tyr Arg
405 410 415 Thr Ser His Gly Arg Ser Asn Met Gly Arg Pro Val Arg Arg Ser Ser Ser Met Arg Ser Leu Asp His Leu Arg Pro Glu Gly Gln Ala Leu Asn 435 440 445 Gly Ser Ser Ser Gly Leu Val Ser Leu Gly Ser Leu Gln Leu Gln 450 460 Gln Gln Leu Ala Pro Asp Phe Thr Cys Asp Cys Ala Ala Gly Trp Thr 465 475 480Gly Pro Thr Cys Glu Ile Asn Ile Asp Glu Cys Ala Gly Gly Pro Cys 485 490 495 Glu His Gly Gly Thr Cys Ile Asp Leu Ile Gly Gly Phe Arg Cys Glu Cys Pro Pro Glu Trp His Gly Asp Val Cys Gln Val Asp Val Asn Glu Cys Glu Ala Pro His Ser Ala Gly Ile Ala Ala Asn Ala Leu Leu Thr 530 540 Thr Thr Ala Thr Ala Ile Ile Gly Ser Asn Leu Ser Ser Thr Ala Leu 545 550 555 560 Leu Ala Ala Leu Thr Ser Ala Val Ala Ser Thr Ser Leu Ala Ile Gly 565 570 575 Pro Cys Ile Asn Ala Lys Glu Cys Arg Asn Gln Pro Gly Ser Phe Ala 580 585 590 Cys Ile Cys Lys Glu Gly Trp Gly Gly Val Thr Cys Ala Glu Asn Leu 595 600 605 Asp Asp Cys Val Gly Gln Cys Arg Asn Gly Ala Thr Cys Ile Asp Leu

Val Asn Asp Tyr Arg Cys Ala Cys Ala Ser Gly Phe Thr Gly Arg Asp 625 630 635 640 Cys Glu Thr Asp Ile Asp Glu Cys Ala Thr Ser Pro Cys Arg Asn Gly
645 650 655 Gly Glu Cys Val Asp Met Val Gly Lys Phe Asn Cys Ile Cys Pro Leu 660 665 670 Gly Tyr Ser Gly Ser Leu Cys Glu Glu Ala Lys Glu Asn Cys Thr Pro 675 680 685 Ser Pro Cys Leu Glu Gly His Cys Leu Asn Thr Pro Glu Gly Tyr Tyr 690 695 700 Cys His Cys Pro Pro Asp Arg Ala Gly Lys His Cys Glu Gln Leu Arg 705 710 715 720 Pro Leu Cys Ser Gln Pro Pro Cys Asn Glu Gly Cys Phe Ala Asn Val Ser Leu Ala Thr Ser Ala Thr Thr Thr Thr Thr Thr Thr Thr Ala 740 745 750 Thr Thr Arg Lys Met Ala Lys Pro Ser Gly Leu Pro Cys Ser Gly 755 760 765 His Gly Ser Cys Glu Met Ser Asp Val Gly Thr Phe Cys Lys Cys His 770 775 780 Val Gly His Thr Gly Thr Phe Cys Glu His Asn Leu Asn Glu Cys Ser 785 790 795 800 Pro Asn Pro Cys Arg Asn Gly Gly Ile Cys Leu Asp Gly Asp Gly Asp 805 810 815 Phe Thr Cys Glu Cys Met Ser Gly Trp Thr Gly Lys Arg Cys Ser Glu 820 830 Arg Ala Thr Gly Cys Tyr Ala Gly Gln Cys Gln Asn Gly Gly Thr Cys 835 840 845 Met Pro Gly Ala Pro Asp Lys Ala Leu Gln Pro His Cys Arg Cys Ala 850 855 860 Pro Gly Trp Thr Gly Leu Phe Cys Ala Glu Ala Ile Asp Gln Cys Arg 865 870 875 880 Gly Gln Pro Cys His Asn Gly Gly Thr Cys Glu Ser Gly Ala Gly Trp

							212.	,,,,	J 1 2 J					
Phe	Arg Cy	s Val 900	Cys	Ala	Gln	GТу	Phe 905	Ser	Gly	Pro	Asp	Cys 910		Ile
Asn	Val As 91		Cys	Ser	Pro	G1n 920	Pro	Cys	Gln	Gly	G1y 925	Аla	Thr	Cys
Ile	Asp G7 930	y Ile	Gly	Gly '	Tyr 935	Ser	Cys	Ile	Cys	Pro 940	Pro	Gly	Arg	нis
G1y 945	Leu Ar	g Cys	Glu	11e 950	Leu	Leu	Ser	Asp	Pro 955	Lys	Ser	Ala	Cys	Gln 960
Asn	Ala Se	r Asn	Thr 965	Ile	Ser	Pro	Tyr	Thr 970	Ala	Leu	Asn	Arg	Ser 975	Gln
Asn	Trp Le	u Asp 980	Ile	Ala	Leu	Thr	Gly 985	Arg	Thr	Glu	Asp	Asp 990	Glu	Asn
Cys	Asn Al 99		۷a٦	Cys	Glu	Asn 1000	G1 <sub>2</sub>	y Thi	r Sei	r Ar	g Cy 10	s T 05	hr A	sn Lei
Trp	Cys G 1010	ly Le	u Pro	Asn	Cys 101	5 T) L5	yr L	ys Va	al As	sp Pi	ro 020	Leu	Ser	Lys
Ser	Ser A 1025	sn Le	u Ser	Gly	Va 1	I C <u>y</u> 30	ys L	ys G	ln Hi	is G	lu 035	۷a٦	Cys	Val
Pro	Ala L 1040	eu Se	r Glu	Thr	Cys 104	5 Le 15	eu S	er Se	er Pi	ro C 1	ys 050	Asn	val	Arg
Gly	Asp C 1055	ys Ar	g Ala	Leu	G]u		ro S	er A	rg Ai	rg Va 10	a1 065	Ala	Pro	Pro
Arg	Leu P 1070	ro Al	a Lys	Ser	Ser 107	7 C <u>y</u>	ys T	rp Pi	ro As	sn G 10	ln 080	Ala	val	Val
Asn	Glu A 1085	sn Cy	s Ala	ı Arg	Leu 109	u ⊤l 90	hr I	le L	eu Le	eu A	1a 095	Leu	Glu	Arg
Val	Gly L 1100	ys Gl	y Ala	. Ser	Val	l G <sup>*</sup>	lu G	ly L	eu Cy	ys S 1	er 110	Leu	val	Arg
۷al	Leu L 1115	eu Al	a Ala	ı Gln	Leu 112	50 I	le L	ys L	ys Pi	ro A	la 125	Ser	Thr	Phe
Gly	Gln A 1130	sp Pr	o Gly	/ Met	Leu 113	и М 35	et V	al L	eu Cy		sp 140	Leu	Lys	Thr
GТу	Thr A	sn As	p Thr	'Val	G]u 115		eu T	hr V	al Se	er S	er 155	Ser	Lys	Leu

							-		55.5	23				
ASI	1160	Pro	o Gli	n Leu	ı Pro	val 1165	Ala 5	a va	l Gly	/ Leu	Leu 1170	Gly	/ Glu	ı Leu
Leu	Ser   1175	Ser	arç	g Glr	ı Leu	1 Asn 1180	Gly	/ Ile	e Glr	ı Arg	1185	Lys	G]ı	ı Leu
G٦ι	1190	Glr )	n His	s Ala	Lys	Leu 1195	Ala	ı Ala	ı Lei	ı Thr	ser 1200	Ile )	val	Glu
۷al	Lys 1205	Leu	ı Glu	ı Thr	' Ala	Arg 1210	∨a <b>1</b> )	Ala	a Asp	Gly	Ser 1215	Gly	His	Ser
Leu	Leu 1220	Ile	e Gly	/ Val	Leu	Cys 1225	Gly	′ ∨al	Phe	Ile	Val 1230	Leu )	∨a1	Gly
Phe	Ser 1235	Val	Phe	: Ile	Ser	Leu 1240	Tyr	Trp	Lys	Gln	Arg 1245	Leu	∆la	. Tyr
Arg	Thr 1250	Ser	Ser	·Gly	Met	Asn 1255	Leu	Thr	Pro	Ser	Leu 1260	Asp	Ala	Leu
Arg	His 1265	Glu	Glu	Glu	Lys	Ser 1270	Asn	Asn	Leu	Gln	Asn 1275	Glu	Glu	Asn
Leu	Arg 1280	Arg	Tyr	Thr	Asn	Pro 1285	Leu	Lys	Gly	Ser	Thr 1290	Ser	Ser	Leu
Arg	Ala 1295	Ala	Thr	Gly	Met	Glu 1300	Leu	Ser	Leu	Asn	Pro 1305	Ala	Pro	Glu
Leu	Ala 1310	Ala	Ser	Ala	Аlа	Ser 1315	Ser	Ser	Αla	Leu	Нis 1320	Arg	Ser	Gln
Pro	Leu 1325	Phe	Pro	Pro	Cys	Asp 1330	Phe	Glu	Arg	Glu	Leu 1335	Asp	Ser	Ser
Thr	Gly 1340	Leu	Lys	Gln	Ala	His 1345	Lys	Arg	Ser	Ser	Gln 1350	Ile	Leu	Leu
ніѕ	Lys 1355	Thr	G∏n	Asn	Ser	Asp 1360	Met	Arg	Lys	Asn	Thr 1365	۷al	Glу	Ser
Leu	Asp 1370	Ser	Pro	Arg	Lys	Asp 1375	Phe	Gly	Lys	Arg	Ser 1380	Ile	Asn	Cys
Lys	Ser 1385	Met	Pro	Pro	Ser	ser 1390	Gly	Asp	Glu	Gly	Ser 1395	Asp	۷al	Leu
Ala	Thr <b>14</b> 00	Thr	Val	Met	۷al									

<211> 17 <212> PRT

<213> artificial/unknown

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<220>
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Arg
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Arg Asp Asp Phe Phe 20
<210> 11
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<223> JAG-1 Notch ligand

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Arg

<210> 12

<211> 19

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<223> r-JAG1 Notch ligand

<400> 12

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Arg Asp Asp

<210> 13

<211> 17

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<220>

<221> misc\_feature

<223> Scrambled JAG peptide

<400> 13

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Phe
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agttgagggg actttcccag gc
                                                                         22
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<223> Human Notch repeats 11-12 - a Notch antagnoist polypeptide
<220>
<221> exon
<222> (1)..(282)
<223>
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<221> misc_feature
<222> (1)..(33)
<223> encodes a tag that is dispensible for Notch antagnoistic activity
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	tgc : Cys :	tcg Ser	ctg Leu	ggt Gly 20	gcc Ala	aac Asn	ccc Pro	tgc Cys	gag Glu 25	cat His	gcg Ala	ggc Gly	aag Lys	tgc Cys 30	atc Ile	aac Asn	96	į
	acg ( Thr I	ctg Leu	ggc Gly 35	tcc Ser	ttc Phe	gag Glu	tgc Cys	cag Gln 40	tgt Cys	ctg Leu	cag Gln	ggc Gly	tac Tyr 45	acg Thr	ggc Gly	ccc Pro	144	
	cga i	tgc Cys 50	gag Glu	atc Ile	gac Asp	gtc Val	aac Asn 55	gag Glu	tgc Cys	gtc Val	tcg Ser	aac Asn 60	ccg Pro	tgc Cys	cag Gln	aac Asn	192	
	gac ( Asp / 65	gcc Ala	acc Thr	tgc Cys	ctg Leu	gac Asp 70	cag Gln	att Ile	ggg Gly	gag Glu	ttc Phe 75	cag Gln	tgc Cys	atg Met	tgc Cys	atg Met 80	240	
	ccc ( Pro (	ggc Gly	tac Tyr	gag Glu	ggt Gly 85	gtg Val	cac His	tgc Cys	gag Glu	gtc Val 90	aac Asn	aca Thr	tga	tga			282	
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	<211>	- 9	2															
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	<221>	- M	Misc															
	<222>	. (	(1)(92)															
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	<220>																	
	<221>		Misc															
	<222>			(11)														
	<223>			eque	nce	for	data	ctin	a no	lvno	ntid	^						
	12257	_	ug J	cquc	iicc		uece	CCIII	g po	Type	ptiu	e						
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	<222>	(:	12).	. (92	)													
	<223>	h	uman	Not	ch r	epea	ts 1	1 an	d 12									
	<400>	16	5						Da	ao 1	2							

Met Ala Ala Glu Phe His His His His His His Gln Asp Val Asp Glu Cys Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Gly Tyr Glu Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr

<210> 17

<211> 249

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<221> exon

<222> (1)..(249)

<223> Encodes human Notch repeats 11-12

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<211> 81

<212> PRT

<213> Artificial/Unknown

<220>

<221> misc

<222> (1)..(81)

<223> Human Notch repeats 11 and 12 - functions as Notch antagonist

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Gly Lys Cys Ile Asn Thr Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln  $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$ 

Gly Tyr Thr Gly Pro Arg Cys Glu Ile Asp Val Asn Glu Cys Val Ser 35 40 45

Asn Pro Cys Gln Asn Asp Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe 50 60

Gln Cys Met Cys Met Pro Gly Tyr Glu Gly Val His Cys Glu Val Asn  $65 \phantom{00}$  70  $\phantom{00}$  75  $\phantom{00}$  80

Thr